INSTRUCTION FOR USE FOR THE HEALTH PROFESSIONAL

Antivipmyn® Tri

Polyvalent antivenom drug

Solution

780 LD50 / 220 LD50 / 200 LD50

Injectable

I. THERAPEUTIC INDICATIONS:

For the treatment of snake bite poisoning:

- ***Crotalus durissus terrificus***, *Crotalus durissus* (Rattlesnake, pig snout, tziripa, saye, tropical rattlesnake, shunu, tzab-can, etc.).
- ***Bothops asper, Bothrops atrox*** (Nauyaca, four noses, yellow beard, velvet, equis, mapana, jararaca, toboba, bone tail, tree viper, green viper, royal nauyaca, river nauyaca, chatilla nauyaca, lever, lever lora , deaf viper, tepoch, ergot, nescascuatl, torito, cha-can, etc.).
- ***Bothrops neuwiedii, Bothrops alternatus*** (urutu), ***Bothrops jararacussu, Bothrops venezuelensis, Bothrops pictus, Bothrops brazili.***
- ***Lachesis muta stenophrys, Lachesis muta muta*** (Machaco lora, mute rattlesnake, rieca, warty, surucucu, lorita, patoco, patoquillo.
- ***Sistrurus spp*** (Nine-plate Rattlesnake).
- ***Agkistrodon spp*** (Cantil, zolocuate, mocasín, cantil de agua, castellana, cumcoatl, metapil, puchucuate, volpoch, etc).

These snakes produce venom (toxin) that can cause serious injuries and even death, **Antivipmyn® Tri** is a product to neutralize the venom of these snakes.

If after the snake bite, any of the following signs or symptoms are observed, the rapid administration of **Antivipmyn® Tri** and transfer to the nearest Hospital or Clinic is recommended:

- Traces of fangs (commonly in pairs).
- Pain, redness and swelling around the bitten area, of varying intensity that may even extend to the affected limb.
- Nausea and vomiting.
- Blisters with opal or bloody liquid content.
- Sensation of numbness around the mouth.
- Hemorrhage of variable intensity both from the bite holes and from the mouth, nose or anus. Presence of blood in the urine.
- Altered coagulation tests and other laboratory determinations.

II. HYGIENIC-DIETARY INDICATIONS

Do not administer liquids or food orally.

There is a risk of asphyxia due to aspiration, mainly in the moderate to severe degrees of intoxication.

III. DOSE AND ROUTE OF ADMINISTRATION:

The route of administration is intravenous, diluting the dose to be administered in 0.9% isotonic saline.

The number of bottles marked as the initial or support dose (depending on the degree of poisoning), should be diluted and transferred to 500 ml of 0.9% isotonic saline solution, in adults and 250 ml in children, it should be administered by drip for 30 minutes. Assess the need to administer a support dose.

There is no preset maximum dose limit, the necessary ones must be applied to neutralize the poison.

Mark the bitten limb in three or four different points, measure its circumference and frequently measure them again, to assess the increase or decrease in inflammation, the decrease indicates a good prognosis.

The improvement of the patient is characterized by lessening the alterations in coagulation, the edema stops, and the CPK tends to normalize since the myonecrosis has finally ceased.

If a laboratory is not available and creatophosphokinase (CPK) cannot be determined, the maintenance dose to be used is the one that managed to stop the edema and this dose should be used every 4 hours.

Preparation of the solution for intravenous application with physiological saline.

Prepare the Antivipmyn® Tri vials to be administered each time, as follows:

1. Remove the small metal disc labeled "OPEN HERE" on the top of the **Antivipmyn® Tri** vial.
2. Using an alcohol swab, clean the rubber stopper that is exposed when the cap marked "OPEN HERE" is removed.
3. Open the vial and with a sterile syringe (10 mL) and needle, withdraw the liquid from the vial and inject it into the vial through the rubber stopper.
4. Remove the syringe and cover the needle with the cap.

5. Shake the vial vigorously until you see that the powder is completely diluted. If you touched the rubber stopper, clean it again.
6. Reinsert the needle with the syringe into the rubber stopper of the vial and remove all of the solution contained in the vial.
7. Remove the needle with the syringe from the vial.
8. Repeat the above steps to open and prepare all **Antivipmyn® Tri** vials to be administered.
9. From the saline bottle, remove the metal or plastic cap on top, exposing the rubber stopper.
10. Clean it with a small piece of alcohol swab.
11. Take the syringe and needle containing the **Antivipmyn® Tri**, insert the needle into the rubber stopper of the bottle with physiological solution and discharge the syringe. Repeat this maneuver with as many bottles with **Antivipmyn® Tri** solution you have prepared.
12. Carefully read the instructions for use of the infusion set (equipment for application in the vein), consisting of thin plastic tubes and needles.
13. Apply a ligature, preferably on the arm to make the vein stand out and become visible.
14. In the vein of the tied arm, insert the needle of the infusion equipment, remove the ligature, fix the needle on the skin and proceed to regulate the speed with which the physiological saline passes, approximately for 4 h (between 30 and 40 drops per minute).
15. For the administration of the support dose, proceed as described in these 15 points.

DOSE

The initial or maintenance dose, depending on the degree of poisoning, will be administered at the following dose, for as long as necessary:

DEGREE OF POISONING	SYMPTOMS (CLINICAL STATUS)	ADULTS		CHILDREN	
		INITIAL DOSE	SUPPORT DOSE	INITIAL DOSE	SUPPORT DOSE
SUSPICION	History of recent snake bite, fang prints, and local pain.	**OBSERVATION**			
GRADE 1 OR MILD	History of recent bite, by a viper, fang prints, bleeding from the bite holes, pain around the bitten area, swelling of 10 cm or less in diameter in the affected limb.	3 to 5 Bottles I.V.	5 Bottles I.V.	6 to 10 Bottles I.V.	5 Bottles I.V.

GRADE 2 OR MODERATE	Same symptoms as Grade 1, but more pronounced, inflammation of 10 cm or more in the affected limb, nausea, vomiting, blisters with whitish or bloody liquid content, decrease in the amount of urine. If there is a laboratory, the coagulation tests and other laboratory determinations are altered.	6 to 10 Bottles I.V.	5 Bottles I.V.	15 Bottles I.V.	5 Bottles I.V.
GRADE 3 OR SEVERE	The same symptoms as Grade 2, more pronounced and also presence of blackish tissue, smelly (dead tissue) in the bitten limb or area, abdominal pain, bleeding from the nose, mouth and / or anus, or all of them, presence of blood in urine and laboratory tests very altered.	11 to 15 Bottles I.V.	6 to 8 Bottles I.V.	20 to 30 Bottles I.V.	10 to 15 Bottles I.V.
GRADE 4 OR VERY SEVERE	The same symptoms as Grade 3 but more pronounced, and accompanied by alterations of various organs and loss of consciousness.	16 or more Bottles I.V.	8 or more Bottles I.V.	31 or more Bottles I.V.	16 or more Bottles I.V.

At the end of the initial dose, assess the need for a support dose and repeat the medical evaluation every 4 hours.

Laboratory criteria to consider: hematic biometry, platelets, PT, PTT, fibrinogen, blood chemistry, serum electrolytes, creatine phosphokinase (evaluate every 4 to 6 hours).

IV. CONTRAINDICATIONS

Known cases of allergy to F (ab')$_2$ fragments of antivenom polyvalent immunoglobulin

V. GENERAL PRECAUTIONS

What to do when faced with a viper bite

Viper bite poisoning is an emergency that must be managed in a hospital environment, even when the product has been previously administered to the patient.

In a recently bitten patient with fangs and without symptoms, he should be observed for at least 15 h; tranquilize him, and splint or immobilize the affected limb, using a sling, to reduce the spread of the venom, since the movement of the affected limb allows its greater diffusion through the general circulation. At the slightest manifestation of intoxication, the administration of **Antivipmyn® Tri** should be started.

No tourniquet should be applied to the bitten limb, or suction or cut over the bitten area. These maneuvers are not helpful, they can cause secondary infections, and aggravate inflammation, leading to more serious injuries.

Any kind of ring, bracelet or tight garment that can interrupt blood circulation, as they accentuate inflammation, should be removed.

Do not administer, liquids or food orally because, there is a risk of asphyxia by bronchial aspiration, mainly in moderate to very severe degrees of intoxication

Recommendations for the administration of Antivipmyn® Tri:

- The sooner **Antivipmyn® Tri** is applied, the better the result.
- The dose in children tends to be higher, because the concentration of the poison is higher in them, because they are smaller and weigh less than adults.
- If the patient has a tourniquet, it should be removed slowly, progressively loosening it while **Antivipmyn® Tri** is administered.
- It is recommended to apply with **Antivipmyn® Tri** support therapy with saline, antibiotics, and tetanus toxoid. Never NSAID-type analgesics such as acetylsalicylic acid, indomethacin, piroxicam, ibuprofen, diclofenac, naproxen, etc., since they potentiate the bleeding caused by snake venom. Metamizole, tramadol, dextropropoxyphene can be used.
- Even when the patient is treated late, the application of **Antivipmyn® Tri** is useful to neutralize the active fractions of the venom.
- Surgical management must be preceded by sufficient administration of **Antivipmyn® Tri**.
- Fasciotomy is recommended only in the presence of compartment syndrome with increased tissue pressure.
- A maximum dose is not established, the necessary ones should be applied to neutralize the poison.
- **Antivipmyn® Tri** is made from equine plasma and therefore may contain infectious agents, for example viruses.

- **Localized reactions and generalized myalgias have been reported from the use of cresol.**

VI. SECONDARY AND ADVERSE REACTIONS

In very sensitive people, it is possible that allergic reactions such as hives, itching, joint pain, slight increase in fever (fever not greater than 37.9 °C) may occur. In such cases, administer antihistamines, if they do not disappear and the patient is not being treated by a doctor, take him immediately to the nearest Health Center or Hospital.

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VII. USE RESTRICTIONS DURING PREGNANCY AND LACTATION

In the event that a pregnant woman is bitten by a snake, the application of **Antivipmyn® Tri** should be done as soon as possible to avoid going into labor or the product dying within the womb.

Breastfeeding should be suspended and **Antivipmyn® Tri** should be administered immediately, because the woman cannot breastfeed the child due to the severity of the poisoning, once the danger has disappeared, resume breastfeeding.

VIII. DRUG INTERACTIONS

Non-steroidal anti-inflammatory analgesics (NSAIDs) should not be used, since they potentiate the hemorrhagic action of the venom.

To date, no interactions have been reported with other medications such as: antihistamines, antibiotics, hydroelectrolytic solutions, antihypertensives, insulin, oral hypoglycemic agents, central-type analgesics, tetanus toxoid and human hyperimmune anti-tetanus immunoglobulin.

IX. FOOD AND BEVERAGE INTERACTIONS

In the moderate and severe degrees of severity, they cannot eat food for the duration of the severity state; therefore, it is not possible to determine interactions with food. The experience with the use of this product indicates that once the patient improves from his poisoning, the patient usual diet can be established.

X. LEGENDS OF PROTECTION

Do not administer if the closure has been violated.
Do not administer if the solution is not clear, if it contains suspended particles or sediment.
The sterility of this medicine is not guaranteed if the packaging shows signs of having suffered previous breakage.
This medicine may contain traces of albumin and cresol that can cause hypersensitivity reactions.
This medicine is prepared from equine plasma that can transmit infectious agents such as viruses.
Report suspected adverse reaction to the mail: farmacovigilancia@cofepris.gob.mx and farmacovigilancia@silanes.com.mx

XI. LABORATORY NAME AND ADDRESS

Made in Mexico by:
Laboratorios Silanes, S.A. de C.V.
Eje 3 Norte Esq. Prolongación 6 Norte No. 200,
Km 52.8, Parque Industrial Toluca 2000, CP 50200,
Toluca, Mexico, Mexico.

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XII. REGISTRATION NUMBER OF THE MEDICINAL PRODUCT WITH THE SECRETARY

Reg No. 58583 SSA-IV